for a 70 kg human. The interferon is administered to a mammal which has a viral infection and is used for treating the infection, as opposed to mere prophylaxis. The oromucosal administration is in a manner which does not involve direct action of the interferon on virally infected cells. Furthermore, when the condition is a rhinovirus, the interferon is not administered through the mouth by multiple or continuous dosages.

Claims 7 and 21-35 have been rejected under 35 USC 103(a) as being unpatentable over Hayden for reasons of record. The examiner states that Hayden teaches the application of interferon for treating rhinovirus infection and other respiratory viral infections using a single treatment by intranasal drops. The examiner states that applicants' comments about Hayden being only for prophylactic application have been noted, but the examiner notes Table 2 on page 547, second study, in which it appears that two of the treated patients had colds. The examiner further points to the disclosure at page 549 that "it remains to be determined whether long-term intranasal adminisration of IFN-α2 will be safe and well tolerated or if IFN-α2 will be useful in the treatment of established colds." The examiner states that this statement is the next logical step in the treatment of

the common cold and a showing over the prior art is needed. This rejection is respectfully traversed.

It is respectfully submitted that the examiner has misinterpreted Table 2 of Hayden. The examiner refers to study 2, IFN treatment, indicating "2/14 (14)" in the column "No. with colds/total no. exposed (%)" and "2/14((14)" in the column headed "No. with colds and infection/total no. exposed (%)". The examiner interprets this as meaning that two people with colds were treated with interferon. However, this is not what the table is intended to show. If one studies the treatment protocol, it is abundantly clear that none of the volunteers entering the protocol had colds. They were then given a preventive dose of interferon or a placebo, and then subjected to rhinoviruses. Some time thereafter, it was determined whether they had developed colds or whether the interferon had protected them. Thus, the third column shows the ratio of the number of people who developed colds to the total number who had been exposed to the virus but that had not yet had cold symptoms. In study 1, 50% of the placebos developed colds, and, in study 2, 57% of the placebos developed colds. However, with interferon, only 17% or 14% developed colds. Thus, the "2/14" means two people of the fourteen in the test <u>developed</u> a cold in the course of the procedure after having been infected with rhinovirus, not that

these people had a cold at the time that the interferon was administered.

To verify that none of the people had colds when administered with the interferon, the examiner's attention is invited to the first paragraph in the first column of page 544, where it states:

> Fifty-five healthy adult volunteers were included in two separate studies ... . Individuals who had an upper respiratory illness or fever within two weeks or who were currently taking intranasal or oral medications (except theophyllines among asthmatics or oral contraceptives) were excluded from participation.

Clearly, therefore, none of the people to whom interferon was administered had an upper respiratory illness or fever. The whole purpose of the test was to test prevention, not treatment.

With respect to the examiner's comment about the statement on page 549 that it remains to be determined whether IFN-α2 will be useful in the treatment of established colds, there is nothing in this statement which would lead to any predictability that IFN-α will be useful in the treatment of established colds. It is merely a statement that this is something that should be tested. In any event, the laboratory of the same authors performed experiments to establish whether or not IFN-α2 would be useful in the treatment of established colds and they reported that it was not. Attached hereto is a

copy of Hayden et al, "Intranasal Recombinant Alfa-2b Interferon Treatment of Naturally Occurring Common Colds", Antimicrobial Agents and Chemotherapy 32(2):224-230 (1988). The effect of this treatment is succinctly stated as follows in the last sentence of the abstract:

> Nasal sprays of recombinant alfa-2b interferon were not an effective treatment for natural colds and were associated with toxicity.

Also attached is an editorial from the British Medical Journal: Scott "Interfering with the Real Cold", Br Med J (Clin Res Ed) 292(6533):1413-1414 (1986). Note the first sentence thereof, where it states:

> Intranasal sprays of interferons are effective in volunteers in preventing experimental colds due to rhinoviruses, but they have no appreciable benefit when given after the symptoms have begun.

Accordingly, those of ordinary skill in the art reading the invitation in Hayden 1983 that it would be useful to see whether IFN-α2 is useful in the treatment of colds, and aware of this laboratory's subsequent publication in Hayden 1988 that administration of IFN-α2 is ineffective in the treatment of established colds, would find no motivation to make or use anything within the scope of the present claims. Accordingly, reconsideration and withdrawal of this rejection are respectfully urged.

In order to expedite allowance of this case, applicant wishes to bring to the examiner's attention the Eby patent 5,286,748, which is of record in this case, but has not been applied in any rejection to date. In order to preempt a possible rejection of the claims over Eby or Hayden (1988), discussed above, applicant proposes to amend claim 7 (by replacing it with new claim 36) to insert two provisos. The first is that the oromucosal administration is in a manner which does not involve direct action of the interferon on virally-infected cells. This language is supported by the last paragraph on page 20 of the specification, and particularly in lines 23-24. This will avoid a technical anticipation by the failed experiments of Hayden (1988). The second proviso is that, when the condition is rhinovirus, the interferon is not administered through the mouth by multiple or continuous doses. This proviso is stated in order to avoid a possible new rejection of unamended claim 7 over the Eby patent, which is already of record in this case. Eby specifically states at column 5, lines 43-53:

> This inventor teaches that all ... interferons ... must be administered to the roof of the mouth, the interior cheeks of the mouth, the tongue, the oromucosa, the oropharyngeal mucosa and all other interior surfaces of the mouth and to the throat, about each one to three hours, in a suitable manner and in a sustained way for any common cold treatment to be effective.

This is a clear teaching that sustained administration, each one to three hours, is required in order to be effective. For the present invention, only a single daily dose of administration is necessary (see page 7, line 1, of the present specification). This difference is because Eby believes that his invention is operable because of "absorption" of the interferon (column 1, line 47) into the lymphatic system or otherwise to circulate into the nasal tissue in the locus of infection (column 4, lines 14-15). On the other hand, the present invention does not act by direct action of exogenously administered interferon, as the interferon does not enter the circulatory system. It acts by stimulation of the lymphoid tissues surrounding the nasal, pharyngeal and oral cavities (see the last paragraph on page 20 of the present specification).

Note also column 5, lines 27-42, of Eby, which states:

> [T]his inventor now teaches that the reason all ... interferons ... fail or produce limited results is because they are not applied to the lining of the mouth in a sustained and repeated fashion, rather they are applied to the more logical and more obvious treatment locus, the interior of the nose, or by a secondary route such as oral ingestion or by injection.

Thus, Eby specifically teaches that the procedure will fail if administered to the interior of the nose. On the other hand,

administering to the interior of the nose is clearly one of the approved means of getting the interferon to the oromucosal cavity in the present invention, as this is what is done in the specific examples. Accordingly, the proviso avoids anticipation by Eby. Furthermore, it would not be obvious to administer interferon to the nose or in a single dose in view of the above-quoted portions of Eby which indicate that administration to the mouth and in a sustained or repeated fashion is critical to effectiveness.

Provisos eliminating disclosed species of a claimed genus to avoid reading on the prior art were held to comply with the written description requirement in *In re Johnson*, 194 USPQ 187, 196 (CCPA 1977).

If applicant had not amended claim 7 (by replacing it with new claim 36), the outstanding rejection would have been overcome for the reasons discussed above. Accordingly, if the examiner wished to reject claim 7 over Eby, for example, the examiner would have had to issue a new non-final official action in order to do so. If the examiner had done this, applicant would have had the opportunity to insert the Hayden (1988) reference in an Information Disclosure Statement and to amend the claims at will. As applicant is merely avoiding these two steps by preemptively amending the claims, it is respectfully requested that the examiner enter and

consider the amendment, notwithstanding the fact that the application is under final. It is further requested that the examiner officially cite of record on a form PTO-892 the Hayden 1988 reference, which is merely attached hereto and cited as evidence of unobviousness. It is also requested that the examiner take notice of copending application no. 08/853,292 which is related to the present application and has the same effective filing date.

It is submitted that all the claims now present in the case clearly define over the references of record. Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

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